IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

CHUGAI PHARMACEUTICAL CO., LTD.,	)	
	)	
Plaintiff,	)	
	)	
v.	)	C.A. No. _____
	)	
ALEXION PHARMACEUTICALS, INC.,	)	**DEMAND FOR JURY TRIAL**
	)	
Defendant.	)	

COMPLAINT

Plaintiff Chugai Pharmaceutical Co., Ltd. ("Chugai"), by its attorneys, for its Complaint against Alexion Pharmaceuticals, Inc. ("Alexion"), alleges as follows:

NATURE OF THE ACTION

1. This is an action for patent infringement and declaratory judgment of patent infringement. Chugai brings this action to protect its intellectual property rights relating to breakthrough medical technologies that it has developed. Chugai has invested heavily in the development of these technologies that provide a benefit to the public by improving the therapeutic qualities of antibody medications. Chugai has developed, for example, a technology that extends the half-life of an antibody in blood plasma, thereby improving the duration of time in which the antibody binds and neutralizes target antigens.

2. Chugai's inventions have wide application in the biotechnology field and in the treatment of diseases requiring administration of therapeutic antibodies. Two such diseases are paroxysmal nocturnal hemoglobinuria (PNH) and atypical hemolytic uremic syndrome (aHUS). These diseases can be fatal, but a patient's quality of life can be improved and symptoms can be managed by medications that inhibit the C5 complement protein. These medications are known

as C5 inhibitors. Chugai's inventions allow patients taking C5 inhibitors to reduce the quantity and frequency of their treatments, leading to improved quality of life for patients.

3. Chugai's technologies are described in and protected by pending patent applications and by U.S. Patent No. 9,890,377 ("the '377 patent" or "the Patent-in-Suit"). A copy of the '377 patent is attached hereto as Exhibit 1. The '377 patent discloses methods of removing an antigen from blood plasma using antibodies modified to take advantage of the weaker antigen-binding activity at the early endosomal pH in comparison with that at the pH of plasma. The modified antibodies are capable of recycling such that they repeat the antigen-binding process multiple times rather than a single time. Chugai and other companies within its strategic alliance are currently developing numerous medicines, including a C5 inhibitor, based on Chugai's patented antibody recycling technology.

4. Defendant Alexion currently markets an FDA-approved therapeutic antibody product known as Soliris (eculizumab). Soliris is a C5 inhibitor prescribed for patients with rare blood conditions like PNH and aHUS. Since its launch in 2007, Soliris has been one of the most expensive drugs in the world.

5. Upon information and belief, in June 2018, Alexion submitted a Biologics License Application ("BLA") to the FDA seeking approval for an improved C5 inhibiting biologic product with a pH-dependent recycling effect. Alexion calls its product "ULTOMIRIS" or ALXN1210" (ravulizumab). Alexion uses the term "ALXN1210" interchangeably to refer to both the ravulizumab antibody and the commercial product containing the ravulizumab antibody. The ALXN1210 product incorporates Chugai's patented recycling technology.

6. Upon information and belief, Alexion intends to market its ALXN1210 product in the U.S. immediately upon receiving FDA approval.

7. Upon information and belief, Alexion's activities in connection with its ALXN1210 product, including manufacturing, importing, using, offering to sell, or selling the ALXN1210 product, are acts of infringement of the Patent-in-Suit, either directly or indirectly, or will be so following approval of the BLA. Chugai files this action to secure a judicial declaration that Alexion will infringe the Patent-in-Suit and to prevent Alexion from any future infringement.

PARTIES

8. Chugai is a biopharmaceutical company based in Japan that has developed many groundbreaking and life-saving medications. These medicines range from cancer drugs like Alecensa®, to the rheumatoid arthritis medication, Actemra®. Chugai scientists also invented emicizumab, a hemophilia A treatment marketed in the United States as Hemlibra®. The FDA has granted multiple "Breakthrough Therapy Designations" for Hemlibra. Chugai's research and development team is committed to creating innovative first-in-class and best-in-class medications for a variety of health conditions.

9. Chugai owns the Patent-in-Suit.

10. Upon information and belief, Alexion is a United States-based biopharmaceutical corporation, incorporated and existing under the laws of Delaware. Alexion maintains a global headquarters at 121 Seaport Blvd., Boston, Massachusetts, 02210.

11. Alexion's global sales of Soliris, a C5 inhibitor, were $1.70 billion in the first half of 2018. Since its FDA approval in 2007, Soliris's global net product sales have exceeded $15 billion. In 2017, more than 88% of Alexion's net product sales were attributable to Soliris. Exs. 2-3.

JURISDICTION AND VENUE

12. This Court has jurisdiction over the subject matter of this action pursuant to 28 U.S.C. §§ 1331 and 1338(a) and the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202.

13. This Court has personal jurisdiction over Alexion because Alexion is incorporated in the State of Delaware, conducts business in Delaware, and has availed itself to rights and benefits under Delaware law.

14. Venue is proper in this Judicial District pursuant to 28 U.S.C. § 1391(b)(1) because Alexion resides in this District.

Alexion Plans To Launch Its ALXN1210 Product Imminently.

15. In Alexion's 10-K for fiscal year 2017, the company stated that "[w]e depend heavily on the success of our lead product, Soliris. If sales of Soliris are adversely affected, our business may be materially harmed. . . . Since we launched Soliris in the U.S. in 2007, substantially all of our revenue has been attributed to sales of Soliris." Ex. 3 at 27.

16. Upon information and belief, Alexion owns U.S. Patent No. 6,355,245, which purportedly covers the Soliris composition of matter and will expire in March 2021. Alexion purports to have other patents protecting its Soliris franchise. Upon information and belief, other pharmaceutical companies are developing biosimilar versions of Soliris in advance of the expiration of the Soliris patents.

17. In order to protect its share of the C5 inhibitor market, particularly in light of the forthcoming expiration of patent protection for Soliris, Alexion has developed an allegedly improved anti-C5 antibody, ALXN1210, which it intends to market as soon as possible. Information published by Alexion confirms that the ALXN1210 product is intended for use in patients suffering from PNH and aHUS. According to Alexion, at least one comparison study has already been conducted between the ALXN1210 product and Soliris. Ex. 4.

18. On June 19, 2018, Alexion announced the submission of the BLA for its ALXN1210 product. *Id.* Alexion further announced that it used a priority review voucher, which designates the BLA for an expedited eight-month review by the FDA instead of the standard 12-month review. In August 2018, the FDA accepted the BLA for its ALXN1210 product for review and set a Prescription Drug User Fee Act ("PDUFA") date of February 18, 2019. That means the BLA for the ALXN1210 product could be approved by mid-February 2019.

19. Upon information and belief, Alexion intends to market its ALXN1210 product in the U.S. immediately upon receiving FDA approval. During an April 26, 2018 earnings call, Alexion Chief Commercial Officer, Brian Goff, stated: "we're formalizing and intensifying all the prelaunch commercialization plans, it's fair to anchor on the ambition which is that we want to make 1210 the new standard of care in PNH." During a July 26, 2018 earnings call, Mr. Goff reiterated: "We continue to charge towards a potential launch in PNH in early 2019 and advance our ALXN1210 pipeline to pursue additional indications, as well as subcutaneous delivery options." Mr. Goff further stated in the July 26, 2018 earnings call: "We're certainly ramping up in our launch preparations [for ALXN1210]."

20. Alexion executives reiterated those comments on October 24, 2018, during a third quarter earnings call with investors. Alexion's CEO, Dr. Ludwig Hantson, said that Alexion is still "actively preparing for anticipated launch" of ALXN1210. Dr. John Orloff, Alexion's head of research and development noted that "we anticipate the approval for 1210 here shortly in the U.S."

21. Upon information and belief, Alexion has used certain of Chugai's patented technologies to develop the ALXN1210 product. Alexion has done so without approval or authorization from Chugai.

THE PATENT-IN-SUIT

U.S. Patent No. 9,890,377

22. The '377 patent, entitled "Antigen-Binding Molecule Capable of Binding To Two or More Antigen Molecules Repeatedly," was issued by the USPTO on February 13, 2018. The patent was issued to Chugai Seiyaku Kabushiki Kaisha as assignee of the named inventors Tomoyuki Igawa, Shinya Ishii, Atsuhiko Maeda, and Takashi Nakai. Chugai Pharmaceutical Co., Ltd. is the English language name for Chugai Seiyaku Kabushiki Kaisha and is the same entity.

23. Chugai's work on the antibody recycling technology described in the '377 patent began before 2010. The '377 patent stems from a series of patent applications claiming priority to a first patent application filed on April 11, 2008. In October 2010, work by Chugai scientists relating to its antibody recycling technology was published in *Nature Biotechnology*. *See* T Igawa et al., *Antibody Recycling by Engineered pH-Dependent Antigen Binding Improves the Duration of Antigen Neutralization*, Nature Biotechnology, 28 (11):1203-07 (2010). *Nature Biotechnology* is a peer-reviewed scientific journal published monthly by the Nature Publishing Group. It is one of the most frequently cited biotechnology publications in the world. The Chugai article was featured on the cover that month.

24. The ’377 patent is directed to methods of removing an antigen from plasma using engineered antibodies with long half-lives in plasma such that the antibodies have improved durations of time in which they can bind to an antigen.

25. The technologies taught by the ’377 patent include technologies that can be used to improve the function of C5 inhibiting antibodies, including those used to treat rare blood diseases like PNH and aHUS.

26. In earlier C5 inhibitor drugs like Soliris, the antibodies contained in the medication bind to the harmful C5 antigens. The antibody and antigen are then internalized by the cell endosome, and degraded by the cell lysosome. This process destroys both the antigen and the antibody such that the antibody performs its function only once before being destroyed. Because the antibody is destroyed in this process, patients taking a drug like Soliris require frequent doses to ensure there are a sufficient number of anti-C5 antibodies in the bloodstream.

27. The ’377 patent teaches methods that allow antibodies to facilitate C5 antigen destruction without also destroying the antibody. This breakthrough allows the antibodies to be “recycled” instead of being destroyed, which will dramatically improve a patient’s quality of life by decreasing the quantity and frequency of drug treatments needed to manage a disease.

DEFENDANT'S INFRINGING CONDUCT

28. The use of Alexion's ALXN1210 product to treat patients does and will continue to implement the technologies taught by and claimed in Chugai's '377 patent.

29. Although the BLA is not publicly available, the properties of the ALXN1210 antibody are described in other publicly available materials. For example, Alexion has described the ALXN1210 antibody in U.S. Patent No. 9,079,949 ("the '949 patent").

30. The '949 patent is entitled "Anti-C5 Antibodies Having Improved Pharmacokinetics." The '949 patent was filed on March 6, 2015, and issued on July 14, 2015. A copy of the '949 patent is attached hereto as Exhibit 5. The '949 patent describes an antibody designated as "BNJ441." On information and belief, the BNJ441 antibody described in the '949 patent is the same antibody as the ALXN1210 antibody.

31. Other Alexion patent applications refer to the BNJ441 antibody. For example, in a PCT application filed by Alexion on January 11, 2017, which was published as WO2017/123636 A1 ("the '636 PCT Application"), BNJ441 is identified as another name for ALXN1210. *See* the '636 PCT Application at 3:14 ("An exemplary anti-C5 antibody is antibody BNJ441 (also known as ALXN1210) ...)." A copy of the '636 PCT Application is attached hereto as Exhibit 6.

32. On information and belief, administration of the ALXN1210 product does and will continue infringe the '377 patent. The '377 patent covers an antibody with a KD(pH5.8)/KD(pH7.4) ratio between, for example, 40 and 10,000. The tested ratio of ALXN1210 is within that range. Ex. 1, Claim 9.

33. Administration of the ALXN1210 product necessarily requires physicians to "identify[…] an individual in need of having an antigen removed from the individual's plasma" and then to "administer[…] the antibody to the individual" as claimed in the '377 patent. Ex. 1.

34. Upon obtaining approval of Alexion's BLA, Alexion will market its ALXN1210 product with product packaging, information, and labeling in accordance with FDA requirements. Such labeling will instruct physicians how to administer the ALXN1210 product in a manner that infringes the '377 patent.

35. In addition, Alexion has stated that one alleged benefit of the ALXN1210 product is that it can be administered once every eight weeks, whereas Soliris treatments must be administered once every two weeks. Ex. 4. This improvement in treatment frequency is consistent with the ALXN1210 product implementing the technologies taught by and claimed in the '377 patent, whereby the half-lives of antibodies in plasma are improved in order to reduce the number of treatments required.

36. Thus, administration of the ALXN1210 product does and will continue to infringe at least one claim of the '377 patent because, upon information and belief, administration of ALXN1210 will necessarily use the methods claimed in the '377 patent.

Alexion Knew Its ALXN1210 Product Infringes the Patent-in-Suit.

37. Prior to and while seeking FDA approval for the ALXN1210 product, Alexion was aware of the '377 patent and/or the underlying patent applications that led to the '377 patent.

38. At least as early as June 2012, Alexion employees read some of Chugai's pending patent applications relating to its antibody recycling technologies, including at least one patent

application that led to the '377 patent. Alexion's review of the Chugai technology prompted Alexion to seek Chugai's permission to use that technology. In 2012 and 2013, Alexion made multiple inquiries regarding obtaining a license to Chugai's antibody technology patents. For example, in July 2012, an Alexion director inquired about obtaining a license to the technology then described in U.S. Patent Application No. 12/936,587. That application led to the '377 patent.

39. Chugai ultimately told Alexion more than once in 2013 that it would not license its antibody recycling technology to Alexion. Specifically, Chugai told Alexion's Vice President of Corporate Strategy and Business Development that Chugai would not license its antibody technologies to Alexion. Chugai is using its recycling and other technologies to develop its own longer-lasting C5 inhibitor product. Chugai's C5 inhibitor product is currently being tested in clinical trials and is called "SKY59." Chugai has not licensed or otherwise authorized the use of its recycling technology by Alexion.

40. Despite knowing that Chugai did not give Alexion permission to use Chugai's recycling technology, and despite knowing that Chugai patented its recycling technology, Alexion knowingly incorporated Chugai's technology into its ALXN1210 product anyway. Alexion's conduct amounts to a willful disregard of Chugai's patent rights. If the ALXN1210 product is approved and Alexion proceeds to manufacture, use, import, offer to sell, or sell the product, Chugai will suffer irreparable harm to its market position as an emerging competitor in the space for C5 inhibitor medication, among other harms.

COUNT I — INFRINGEMENT OF THE '377 PATENT

41. Chugai realleges and incorporates by reference the allegations contained in Paragraphs 1 through 40.

42. On information and belief, Alexion has infringed the '377 patent by engaging in the commercial manufacture, use, offer to sell, sale, or importation into the United States of ALXN1210 before the expiration of the '377 patent and by actively inducing and/or contributing to the infringement of others in violation of 35 U.S.C. § 271(a), (b), (c), or (g).

43. Chugai will be substantially and irreparably harmed if Alexion is not enjoined from infringing the '377 patent.

44. Chugai has no adequate remedy at law.

45. This case is exceptional, and Chugai is entitled to an award of attorneys' fees under 35 U.S.C. § 285.

46. Upon information and belief, Alexion has knowingly and willfully infringed the '377 patent.

COUNT II — FOR DECLARATORY JUDGMENT OF INFRINGEMENT OF THE '377 PATENT

47. Chugai realleges and incorporates by reference the allegations contained in Paragraphs 1 through 46.

48. Upon information and belief, Alexion intends to manufacture, market, sell, offer to sell, and/or import ALXN1210 immediately upon receiving FDA approval.

49. Alexion's submission of a BLA to the FDA, coupled with Alexion's activities in support of its manufacture, importation, and launch of its ALXN1210 product for commercial sale in the United States upon receiving that approval, creates an actual, immediate, and real controversy within the Declaratory Judgment Act regarding Alexion's direct infringement, or active inducement and/or contribution to infringement of, valid and enforceable claims of the '377 patent before its expiration in violation of 35 U.S.C. § 271(a), (b), or (c).

50. The making, using, selling, offering to sell, or importing of the ALXN1210 product will satisfy each element and infringes, literally or under the doctrine of equivalents, one or more claims of the '377 patent, in violation of 35 U.S.C. § 271(a), (b), or (c).

51. Chugai will suffer irreparable harm and loss from Alexion's imminently infringing activities, if not enjoined.

52. Upon information and belief, Alexion will knowingly and willfully infringe the '377 patent.

PRAYER FOR RELIEF

WHEREFORE, Chugai Pharmaceutical Co., Ltd. respectfully requests the following relief:

a. A judgment that the '377 patent has been infringed and will be infringed by Alexion upon launch of its ALXN1210 product in the U.S.;

b. Any available injunctive relief to prevent the commercial manufacture, importation, use, offers to sell, or sale of ALXN1210 pursuant to 35 U.S.C. § 283, 28 U.S.C. § 2202, and FED. R. CIV. P. 65;

c. Any available damages pursuant to 35 U.S.C. § 284, including an award of treble damages;

d. A judgment that this is an exceptional case and that Chugai be awarded its attorneys' fees incurred in this action pursuant to 35 U.S.C. § 285;

e. Costs and expenses in this action;

f. Such other and further relief as the Court deems just and appropriate.

DEMAND FOR JURY TRIAL

Chugai hereby demands trial by jury on all issues so triable.

/s/ Karen E. Keller
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